OFFICE OF ALTERNATIVE MEDICINE
RESEARCH PROTOCOL WORKBOOK

Instructions for completing form: Either type or print neatly. Please respond to each question. Write "na" if not applicable. You may continue your responses on another sheet(s) of paper by attaching to the completed form. When the form is completed, please mail to:

National Institutes of Health
Office of Alternative Medicine
Research Development & Investigation Section
9000 Rockville Pike
Bldg. 31, Room 5B-50
Bethesda, MD 20892

Your Workbook will be reviewed by our staff and you will be contacted after this document has been comprehensively evaluated. Thank You.

I. PRINCIPAL INVESTIGATOR DATA

1) Name: _____
(last) (first) (middle)

2) Address: _____
(street) (city) (state) (zip code)

3) Telephone: _____ **Fax:** _____

4) Email Address: _____

5) List any Co-Investigators: _____

_____

_____

_____

Note: All investigator's must attach a copy of most recent Curriculum Vita with this completed profile form.

6) Do you use CAM in clinical practice? ☐ NO ☐ YES If yes, please specify CAM system/method/technique(s): _____

_____

_____

_____

_____

a) Approximately what percent of your practice time is devoted specifically to CAM: (please circle one)

10 20 30 40 50 60 70 80 90 100%

7) Do you have research experience in CAM? ☐ NO ☐ YES If yes, please specify in what CAM field, and briefly describe the research topic(s) studied (including projects completed & publications): _____

8) Do you have research experience outside of the field of CAM? ☐ NO ☐ YES If yes, please briefly specify the research field and the topic(s) studied (including projects completed & publications): _____

9) Are you presently affiliated with an academic institution (university, private research facility): ☐ NO ☐ YES If yes, please specify the nature of your affiliation:

II. RESEARCH PROPOSAL PLAN

1) Title of Research Proposal: _____

2) Specify the CAM Modality (s) to be studied:

3) Specify the Disease(s) or Condition(s) to be studied:

4) What is the Research Question under consideration (e.g. Should chelation therapy be used in the treatment of coronary artery disease?):

5) Have you conducted a literature search on this research topic? ☐ NO ☐ YES
If you answered no, why have you not yet conducted the literature search?

a) If you answered yes, please attach the bibliography to this form and respond to the following questions and information requests.

b) Write a paragraph justifying this research question based upon the literature you have reviewed. Can you justify the study by clinical experience, tradition, or by whom it may affect? (e.g. The literature justifies the use of conventional therapies for the treatment of coronary artery disease (CAD). These therapies include medicines, angioplasty procedures and coronary bypass surgeries. Great controvery arises over the question of the effectiveness of chelation therapy in the treatment and prevention of CAD. The few available studies supporting the use of chelation therapy have been described as of "poor scientific quality". No study to date has conclusively addressed chelation therapy's role in CAD.):

6) Outline the Study Objectives (e.g. The objective of this clinical study is to systematically evaluate the effect of 30 biweekly intravenous infusions of $Na_2MgEDTA$ campared with placebo in a population of patients with obstructive astherosclerotic coronary artery disease manifested by angina pectoris.):

7) Considering the literature review, reexamine your original research question and answer the following questions:

a) Provide a one sentence study hypothesis (e.g. Magnesium disodium EDTA effectively chelates arterial calcium plaque and will improve the time to moderate angina on a graded multistage exercise treadmill test.):

b) What do you expect to find from this study? (e.g. reduced incidence of CAD and CAD related events in adults with active CAD):

c) What is/are alternative explanation(s) for the expected study outcome(s) just described? (e.g. study participants began regimens of low fat diet and exercise; during the study period, medicines and supplements taken concomitantly and/or behavioral changes such as stress reduction begun): _____

_____

_____

_____

_____

8) Define the patient population you wish to study (e.g. 200 males and females representative all races, ≥ 18 years of age, who have active but stable coronary vascular disease as evidenced by diagnostic ST segments changes on exercise treadmill testing, etc.. Persons will be excluded if s/he is unwilling or unable to cooperate with study porotocol instructions, inability to perform exercise treadmill testing, etc. Study participants will be recruited from the practices of specific chelation therapists as well as cardiologists in a specified geographic region):

a) sample size: _____

b) age range: _____

c) gender: _____

d) race: _____

e) medical history: _____

_____

_____

_____

f) inclusion/exclusion criteria: _____

_____

_____

_____

g) recruitment of patients: _____

_____

_____

_____

9) Define the period of time for the study, recognizing that this may change as protocol is further developed and refined. It is helpful to develop a timetable:	
EXAMPLE:	
One Year Study Period	
6 Months	**6 Months**
Specify Timeline Objectives (e.g. 30 week infusion therapies; Follow-up Evaluation Procedures, etc.)	

10) Define the variables which will be measured and the instruments which will be used to measure them:

EXAMPLE:		
Variables to be Measured	**Measurement Instrument**	**Availability to You Presently?**
1) Cholesterol/Triglyceride Levels	**1) Lab blood analysis**	**1) Yes - clinic lab**
2) Aerobic Caridac Performance	**2) Exercise Treadmill testing**	**2) Yes - hospital**
3) Myocardial Ischemia/ regional cardiac wall motion abnormalities	**3) Exercise Echocardiography**	**3) Yes - hospital**

Variables to be Measured	**Measurement Instrument**	**Availability to You Presently?**

11) Describe your proposed research design (please refer to the attached Summary of Research Study Designs):

12) Does the proposal involve the use of substance (eg herbal) or device which would require approval from a government agency (eg FDA)? ☐ NO ☐ YES If yes,

1) Describe the substance/device:

2) Do you know which approval agency you will need to contact? ☐ NO ☐ YES
If yes, which agency approval is required:

Have you contacted this agency yet? ☐ NO ☐ YES Please explain your answer
including a description of your present status with this agency:

13) If this study involves human subjects, please specify if you have:

a) Contacted your Institutional Review Board (IRB): ☐ **NO** ☐ **YES**
If yes, have you received the IRB documents outlining their specific requirements for human research to be conducted in that institution?
☐ **NO** ☐ **YES**

b) Developed an Informed Consent Form: ☐ **NO** ☐ **YES** **If yes, please attach consent form.**

III. RESEARCH STUDY RESOURCES, ADMINISTRATION AND DATA ANALYSIS

1) With regard to data collection, please specify:

a) Have you developed a data collection form/spreadsheet: ☐ **NO** ☐ **YES**
b) Which computer data base program will you be using to enter data: _____

c) Who will be collecting the data and how? (e.g. after signing the consent forms, the research study nurse will complete a data sheet on each participant and ownload the data into a computer file which will be reviewed and evaluated by the research study investigators.): _____

d) How and where will be data be stored; please specify methods by which data is safeguarded from tampering: _____

e) Describe the means by which the data will be guaranteed as confidential:

2) Describe any potential study bias (defined as the a source of systematic error that may affect your study results) Please refer to the Summary of Study Bias Factors:

TYPE OF BIAS	IMPACT ON STUDY OUTCOME

3) Describe any other sources of bias, not previously mentioned, which may potentially be present and limit your study

4) Describe any limitations to generalizability of your study results (e.g. will a study on chelation therapy in patients with active CAD be applicable to patients at risk for but who do not presently have CAD?)

5) Describe the possible importance and use of your results if, upon completion of the study, they show an outcome which is:

a) Positive:

b) Negative:

6) Please describe any current or pending sources of funding for any ongoing research in which you are participating as an investigator:

7) Please describe any current or pending sources of funding for this research proposal:

RESOURCE INVENTORY:
Please specify whether the following resources are required for your study, and which are presently available:

RESOURCE CATEGORY	PRESENTLY AVAILABLE	NOT PRESENTLY AVAILABLE
	✓	✓
I. PERSONNEL (Must includeCV's/ qualifications)		
Principal Investigator(s)		
CAM practitioner(s)		
Conventional practitioner(s)		
Basic Scientists(s)		
Laboratory Technician(s)		
Support Staff:		
RN		
RNP		
RN Assistant		
PA		
CAM technician		
Consultants/Specialists		
II. PHYSICAL SPACE/LOCATION		
Clinic		
Hospital		
Private Office		
Laboratory		
Speciality Treatment Room(s)		
III. FINANCIAL COSTS		
Personnel		
Treatment		
Administrative (non-personnel)		
Travel		
Hardware: rent/buy		
Computers: rent/buy; soft/hardware		
Library Services		

Appendix A

SUMMARY OF STUDY BIAS FACTORS

A GLOSSARY OF TERMS

CATEGORIES OF BIAS

I. SELECTION - comparisons are made between groups of patients that differ with respect to determinants of the outcome other than those under study.

II. MEASUREMENT - methods of measurement are consistently dissimilar among groups of patients.

- Repeated Measurement

III. CONFOUNDING - two factors or processes are associated or "travel together", and the effect of one is confused with or distorted by the effect of the other.

- Historical Events

IV. INVESTIGATOR - when the research investigator in a position whereby s/he may unintentionally demonstrates an attitude or behavior and perceives the results in a way which allows the data to affirm his/her own hypothesis and research agenda.

V. OTHER

- Effects of Maturation
- Subject Attrition
- Instrument Decay
- Statistical Regression

Appendix B

SUMMARY OF RESEARCH STUDY DESIGN CHARACTERISTICS

A GLOSSARY OF TERMS

STUDY CATEGORIES

I. RETROSPECTIVE

- Cohort
- Epidemiologic Survey
- Consecutive Practice Series

II. PROSPECTIVE

- Cohort
- Epidemiologic Survey
- Prospective Parallel Outcome Study
- Consecutive Practice Series

III. EXPERIMENTAL

- Randomized Double-Blind Trial
- Randomized Placebo Controlled Trial
- Basic Science
- Preclinical Study

IV. CROSS-SECTIONAL

V. DESCRIPTIVE

- Epidemiologic Survey
- Research Summary/Meta-Analysis
- Cost/Benefit Study
- Consecutive Practice Series

VI. OBSERVATIONAL

- Case Control/Case Report
- Cross-Sectional
- Longitudinal
- Consecutive Practice Series

- Multi-Disciplinary???
- Inter/Intra System Research???
- Before/After Clinical Assessments???

Appendix C

Summary Checklist of Guidelines for Protocol Writing *

***Adapted from The N.I.H. Office of Human Subjects Research Information Sheet #5 "Guidelines for Writing Research Protocols" revised 1995 edition.**

✓ IF COMPLETED	REQUIRED PROTOCOL ELEMENT
	TEXT OF THE PROTOCOL
1) _____	**PRECIS:** In a paragraph of 100 words or less, provide a summary of the study, including objectives, study design, study population, and any outcome parameters.
2) _____	**INTRODUCTION:** Provide a background of the study topic, including the natural history and treatment issues; if the study involves a new technique or procedure, describe any preliminary work, including animal data for any Investigational New Drug applications.
3) _____	**OBJECTIVES:** Outline the study questions and goals; include a statement of hypothesis (es), using some of the objectives as hypotheses.
4) _____	**STUDY DESIGN and METHODS:** Describe the following elements: a) human subject involvement_____ b) initial evaluation procedures and screening tests_____ c) any phases, procedures and sequence of the study_____ d) patient population characteristics: inclusion/exclusion criteria____ e) a detailed description of the treatment protocol including doses etc._____ f) any randomization procedures_____ g) investigator credentials as it relates to any experimental or investigational procedures to be done during the study _____
5) _____	**HUMAN SUBJECT MONITORING:** Provide the following data: a) type, frequency and duration of the tests_____ b) any hospital admissions or outpatient visits_____ c) exact stop points for testing in the study_____ d) criteria for human subject withdrawal_____

6)	**ANALYSIS OF THE STUDY:** Describe the: a) precise outcomes to be measured and analyzed_____ b) how the data will be measured and statistically analyzed _____ c) methods to estimate the required number of subjects necessary for the study_____ _____ d) power calculations is the study involves comparisons_____
7)	**HUMAN SUBJECT PROTECTIONS:** Provide the following: a) rationale for research subject selection, based upon a review of gender/ethnicity/race or special class (e.g. children) categories at risk for the disease or condition to be studied_____ b) strategies and procedures for subject recruitment_____ c) justification for exclusion of any subject category_____ d) potential benefits to the subjects from the study_____ e) any compensation offered to the subjects_____ f) potential risks: physical, psychological, social, legal, other_____ g) methods by which the confidentiality of the subject's will be safeguarded_____ h) any necessary interventions which will be taken with the advent of any adverse effects from the study_____ i) data monitoring to ensure subject safety_____ _____ j) a cost/benefit of risks Vs anticipated benefits from the study_____
8)	**INFORMED CONSENT:** This document should be understanable to someone who has not completed high school. The consent form should include the following 8 elelments: a) a statement that the study involves research, with an explanation of the purpose of the research, duration of the subject's participation, the procedures to be followed by the subject, and the identification of any experimental procedures_____ b) a description of any foreseeable risks or discomforts to the subject,an estimate of their likelihood and a description of what steps will be taken to prevent or mitigate them_____ c) a description of any benefits to the subject or to others that may reasonably be expected from the research_____ d) a disclosure of any appropriate alternative procedures or courses of treatment that might be advantageous to the subject_____ e) a statement describing the extent of confidentiality of records including a description of who may have access to research records (e.g. specific individuals, private or publics agencies)_____

_____	f) for research involving more than minimal risk, an explanation and description of any compensation and any medical treatments available if research subjects are injured; where further information may be obtained , and whom to contact in the event of a research-related injury to the subject_____ g) an explanation of whom to contact for answers to pertinent questions about the research and the research subject's rights_____ h) a statement that the participation is voluntary and that refusal to participate or discontinuing participation at any time will involve no penalty or loss of benefits to which the subject is otherwise entitled_____